Using a Life-Stage Approach for Assessment of Children's Health Risk

Stan Barone [1], Rebecca Brown [1, 2], Susan Euling [1], Elaine Cohen-Hubal [3], Carole A. Kimmel [1], Susan Makris [1,4], Hisham El-Masri [1], Jacqueline Moya [1], Sherry G. Selevan [1], Bob Sonawane [1], Tracey Thomas [1, 5], Chad Thompson [1, 5]
[1]NCEA/ORD/EPA, [2]Association of Schools of Public Health, [3]NERL/ORD/EPA, [4]OPPTS/EPA,
[5]American Association for the Advancement of Science

Science Question

What is the basis for differential risk? What are the outcomes that need to be considered in a life-stage focused risk assessment framework? What is the impact of exposure to environmental pollutants throughout development on human health outcomes? How do we incorporate data on susceptible populations into the risk assessment process?

Research Goals

Incorporate into risk assessment a focus on life stage-specific considerations for exposure and effects in order to better characterize the risk to susceptible groups within the population.

Results/Conclusions

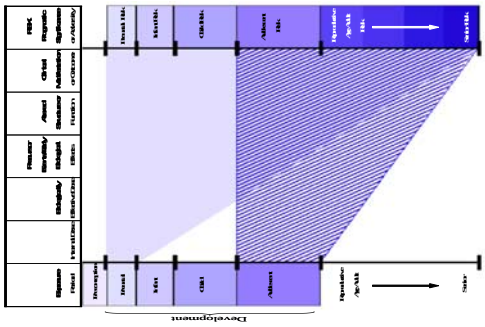
Summary of gap analysis:
- Identify needs for specific areas for guidance
  - Application of developmetal and reproductive outcomes to risk assessments for various durations.
  - Dose-response assessment for developmental data
  - Pharmacokinetic modeling.
  - Life-stage specific application of mode of action to risk assessment
- Identify training needs and training tools.

Impact and Outcomes

This framework addresses the question of why and how an improved children's health risk assessment will strengthen the overall risk assessment process across the Agency. The value added of this approach includes:
1) A more complete evaluation of the potential for vulnerability at different life stages,
2) Evaluation of potential for toxicity after exposure during all developmental life stages,
3) Integration of adverse health effects and exposure information across life stages, and
4) A focus on the underlying biological events and critical developmental periods for incorporating mode of action considerations.

Future Directions

- Get Framework externally reviewed
- Develop chemical specific case studies
- Develop adjunct guidance where needed
- Develop training for Program Offices and other risk assessors
- Apply life stage-specific approach in future assessments.



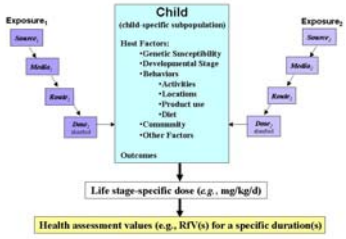
Problem Formulation

Problem Formulation – Planning and Scoping
Consider:
- Purpose
- Scope
- Participants
- Approach
- Resources
- Past Experiences/Assessment Precedents

Discussion of possible outcomes of assessment with risk managers, risk assessment team, stakeholders, and other interested parties

Conceptual Model
Consider:
- Sources
- Receptors
- Stressors
- Pathways (Media, Routes)
- Host Factors
- Outcomes

Analysis Plan
Consider:
- Methods
- Models
- Data Gaps
- Uncertainties and Variability



Analysis

Hazard Characterization

Scoping of Hazard
- Consider:
  - Available studies
  - Life stage-specific exposures, assessments, and outcomes

Identify Studies

Review Individual Studies
- Consider:
  - Study purpose, design, and exposures
  - Outcomes
  - Toxicokinetics & toxicodynamics (MOA)
  - Qualitative dose-response relationships for adverse outcomes
  - Uncertainties

Characterization the Hazard Database
- Summarize the database
- Conduct weight-of-evidence assessment:
  - Control of confounders, effect modifiers
  - Toxicokinetics; toxicodynamics (MOA)
  - Uncertainties and data gaps
  - Extent of the database
  - Interspecies comparisons of outcomes
  - Relevance of animal data to humans

Life Stage-Specific Hazard Characterization
- Consider:
  - Life stage-specific outcomes
  - Scientific Rationale
  - Sensitivity / specificity
  - Variability
  - Uncertainty

As necessary collect more data, conduct more detailed analysis

Dose-Response

Dose-Response Scoping
- Extent of Assessment
  - Directed (life stage(s) of interest)
  - Broader (all life stages are considered)
- Identify Output Needed
  - Risk Endpoints (*e.g.*, RfV, CSF)

Summarize Data & Tools Available

Select Dose-Response Relationship(s)
- Summarize dose-response relationships
- Conceptualize the MOA/Identify dose metric
- Select life stage-specific D-R models (if available) or compile necessary life stage-specific physiological parameter data

Extrapolation & Risk Value Derivation
- Adjust PODs for route, duration, intraspecies, and interspecies factors and/or run PBTK and BBDR models with life stage-specific parameter adjustments
- Derive risk value(s)
- Adjust risk values by appropriate UFs

Life Stage-Specific Dose-Response Characterization
Consider:
- Scientific Rationale
- Variability
- Uncertainty
- Sensitivity

As necessary collect more data, conduct more detailed analysis

Exposure Assessment

Scoping of Exposure Assessment
- Consider:
  - Sources
  - Pathways (media and route)
  - Scenarios

Develop Conceptual Model

Review Available Data
Consider:
- Chemical properties, fate and transport
- Exposure Media Concentrations
- Life Stage-Specific Population Characteristics
- Life Stage-Specific Activity Data

Life Stage-Specific Exposure Analysis
- Select Approach
  - Screening Approach
  - Refined Assessment

Life Stage-Specific Exposure Characterization
- Consider:
  - Scientific Rationale
  - Variability
  - Uncertainty
  - Sensitivity analysis

As necessary, collect more data and conduct more detailed analysis.

Risk Characterization

Synthesis of and integration of hazard, dose response and exposure information.

Summary of uncertainties and assumptions used in assessment including variability and uncertainty in database.

Describe risk context.

epascienceforum
Collaborative Science for Environmental Solutions
2005
epa.gov/scienceforum